Effect of Anesthetics During Oocyte Pick-Up Procedure on Oocyte Quality and Pregnancy

Oosit Pick-Up İşleminde Anesteziklerin Oosit Kalitesi ve Gebelik Üzerindeki Etkileri

Oocyte Pick-up Procedure and Anesthetics

Aykut Urfalıoğlu[1], Aslı Yaylalı[2]
[1]Department of Anesthesia and Reanimation, [2]Department of Histology and Embryology,
Kahramanmaras Sutcu Imam University, School of Medicine, Kahramanmaras, Turkey

Özet

Amaç: Overlerden oosit toplanması olarak tanımlanan, oosit pick-up (OPU) işleminde farklı anestezi yöntemleri kullanılabilmektedir. Genel anestezikler foliküllere geçerek oosit kalitesini etkileyebilmektedir. Merkezimizdeki OPU işlemlerinde anestezikler, işlem ve derlenme süreleri ile estradiol (E2) düzeyleri, toplam, matür (M2) ve fertilize oosit sayıları, gebelik oranlarının retrospektif olarak değerlendirilmesi amaçlandı. Gereç ve Yöntem: OPU nedeniyle anestezi uygulanan hastaların demografik verileri (yaş, boy, kilo, total prosedür süresi), anestezikler ve tüketim miktarları, derlenme süreleri, toplam, M2, fertilize oosit sayıları ve gebelik oranları incelendi. Hastalar indüksiyonda; sadece propofol uygulanan (Grup P) ve propofol-ketamin uygulanan hastalar (Grup PK) olarak 2 gruba ayrıldı. Bulgular: Her iki gruptaki demografik veriler benzerdi. Propofol tüketim miktarları grup P'de 170 (320-120) mg, grup PK'da 140 (190-110) mg idi (p<0,001). Derlenme süreleri, grup P'de anlamlı şekilde kısa bulundu (sırasıyla; 6 (9-3), 7 (10-5)) (p<0.001). Her iki grupta E2 düzeyleri, total, M2, fertilize oosit sayıları benzer olup, istatistiksel fark bulunmadı (sırasıyla; p=0.837, p=0.434, p=0.518, p=0.524). Gebelik oranı grup P'de 32,7% iken grup PK'da 29,1% bulundu (p=0.720). Tartışma: OPU anestezisinde hedef, hızlı derlenme amacıyla optimal dozda anestezik kullanımı sağlamaktır. Ancak anesteziklerin follikül sıvısına geçerek zararlı oldukları bilinmektedir. Kullandığımız ajanların folliküler miktarları ölçülmedi ancak fertilizasyon, gebelik oranları, oosit kalitesini belirgin olarak etkilenmedikleri görüldü. Sonuç olarak, OPU'larda propofol, ketamin, remifentanil ve sevofluran ile yapılan anestezi uygulamasının fertilizasyonu olumsuz yönde etkilemediği düşünüldü.

Anahtar Kelimeler

Oosit Pick-Up; Gebelik; Genel Anestezi; Propofol; Ketamin

Abstract

Aim: Different anaesthesia methods can be used in the oocyte pick-up (OPU) procedure. General anaesthetics may affect the quality of the oocytes by passing into the follicles. The aim of this study was to retrospectively evaluate anaesthetics used in OPU in our centre through examination of procedure and recovery times, estradiol (E2) levels, numbers of total, mature (M2) and fertilised oocytes, and pregnancy rates. Material and Method: The demographic data of patients applied with anaesthesia for OPU were examined together with the anaesthetics and amounts used, recovery time, numbers of total, M2 and fertilised oocytes, and pregnancy rates. The patients were separated into 2 groups as Group P, where only propofol was used in induction, and Group PK where propofol+ ketamine was used. Results: The demographic data were similar in both groups. Propofol consumption was mean 170mg (320-120 mg) in Group P and mean 140mg (190-110 mg) in Group PK (p<0.001). The recovery period was statistically signficantly shorter in Group P (6 mins (9-3) vs 7 mins (10-5)) (p<0.001). In both groups the E2 levels and numbers of total, M2 and fertilised oocytes were similar with no statistically significant difference determined (p=0.837, p=0.434, p=0.518, p=0.524 respectively). The pregnancy rate was 32.7% in Group P and 29.1% in Group PK (p=0.720). Discussion: The aim of OPU anaesthesia is to provide the use of anaesthetic at the optimal dose with rapid recovery. However, the transfer of anaesthetics to follicular fluid is known to be harmful. Although the follicular amounts of the agents used in this study were not measured, there was seen to be no significant effect on fertilisation, pregnancy rates, and oocyte quality. It can be concluded that the application of anaesthesia with ketamine, remifentanyl, and sevofluorane in OPU procedures has no negative effect on fertilisation.

Keywords

Oocyte Pick-Up; Pregnancy; General Anaesthesia; Propofol; Ketamine

DOI: 10.4328/JCAM.4617 Received: 09.05.2016 Accepted: 15.06.2016 Printed: 01.11.2016 J Clin Anal Med 2016;7(6): 840-3
Corresponding Author: Aykut Urfalioğlu, Kahramanmaras Sutcu Imam University, School of Medicine, Avsar Campus, 46100, Kahramanmaras, Turkey.
GSM: +903442803434 F.: +90 3442804052 E-Mail: aykutmd1903@gmail.com

Introduction

Invitro fertilisation (IVF) is an important procedure that has been developed to treat infertility. This procedure consists of these stages: controlled stimulation with drugs administered to the ovaries, transvaginal oocyte aspiration from the ovaries under ultrasound guidance, fertilisation, and transfer of the embryo to the uterus [1]. The procedure of collecting oocytes from the ovarian follicles, known as oocyte pick-up (OPU), was previously performed by laparoscopy under general anaesthesia, but is currently performed under transvaginal ultrasound guidance, in a shorter and less invasive manner [2, 3].

If there is pain caused by the penetration of the needle into vaginal mucosa and the ovarian capsule or if there are other stress factors of differing degrees in patients during the procedure, anaesthesia is required [4]. Various applications, from minimal sedation to deep sedation and general anaesthesia can be applied with neuroaxial techniques such as epidural or spinal anaesthesia and regional block techniques such as paracervical/paraovarian block [1]. Although the choice of method varies according to the centre, generally, in OPU, regional anaesthesia methods are preferred when the patient is awake, or conscious sedation when the patient is co-operative [2, 3, 5]. Several clinical and experimental studies have reported that oocyte quality and pregnancy rates are affected by the transfer of general anaesthetic agents to the follicles aspirated in the ovaries [6, 7]. In patients with a high level of anxiety, deep sedation or general anaesthesia methods are usually required; in patients where general anaesthesia is applied, the level of the anaesthetic drug used can be increased according to the level of anxiety [8, 9].

The aim of this study was to retrospectively evaluate the effects of the anaesthetic drugs used in OPU procedures in our centre by examining the demographic data of the patients, the doses of the drugs, total procedure and recovery times, estradiol (E2) levels, numbers of total, mature (M2) and fertilised oocytes, and pregnancy rates. In addition, it was thought that examination of the existing literature, along with an internal evaluation of our newly-opened centre, would be useful to review and improve our accountability by exposing any deficiencies in the application of anaesthesia in OPU.

Material and Method

Approval for the study was granted by the Scientific Research Ethics Committee of Sütcü Imam University, Kahramanmaras, Turkey (protocol no: 12 – 2016/07). A retrospective review was then made of the records of patients who presented at the Assisted Reproductive Treatment Centre of our hospital between 18/11/2015 and 01/04/2016 for IVF treatment and who were then administered anaestheia for the OPU procedure.

Demographic data such as age, height, weight, and ASA status were noted from the records, together with haemodynamic data, agents used for anaesthesia induction and maintenance and the amounts used, total procedure time (from IV anaesthetic induction to patient awakening with the termination of anaesthetic administered for maintenance following the OPU procedure), recovery time (the period from patient awakening after the procedure to obtaining modified Alderate score ≥8 in the recovery unit) and any complications that occurred. The numbers of total, mature (M2) and fertilised oocytes, and pregnancy rates were also recorded. Patients were excluded from the study if no oocytes were collected during the procedure or if embryo transfer could not be made because there had been no fertilisation.

Routine monitoring (non-invasive blood pressure [NIBP], heart rate [HR], pulse oximetry (SpO_2), 3-lead ECG) was applied to all patients on admittance to the operating room for OPU procedure in our centre. After completion of necessary preparations, 3 IV agents were selected for routine deep sedation. The patients included in the study were retrospectively separated into 2 groups based on these agents. Group P was only administered propofol and Group PK was adminstered a propofol-ketamine combination.

Patients in Group P received 2 mg/kg IV propofol (Propofol 1% amp, Fresenius) and 1 mcg/kg IV remifentanyl (Ultiva 2 mg flk, Glaxo SmithKline) and those in Group PK received 2 mg/kg IV propofol and 0.25 mg/kg IV ketamine (Ketalar 0.5 gr flk, Pfizer) with 1 mcg/kg remifentanyl. In both groups, anaesthesia was maintained with 2% Sevoflurane (Sevorane liquid, Abbott) and a 50%-50% mixture of O_2/air applied by face mask.

Throughout the operation, patients in both groups were administered IV push propofol of 10-20 mg as needed. No other anaesthesia method (neuroaxial block, paracervical block, minimal sedation, intubation with general anaesthesia) or drugs were used. Intraoperative and postoperative complications (laryngeal-bronchial spasm, aspiration, massive bleed, etc.) that developed in the patients were noted in the records.

In the statistical analysis of the variables, the SPSS 22.0 (IBM Corporation, Armonk, NY, USA) software program was used. Conformity to normal distribution of the data was evaluated with the Shapiro-Wilk test and variance homogeneity with the Levene test. In the comparison of 2 independent groups, the Independent Samples t-test together with the Bootstrap results was used and the Mann Whitney U-test with the Monte Carlo simulation technique. In the comparison of categorical variables, the Fisher Exact test was applied. Quantitative variables were stated as mean ± standard deviation (SD) and median with range (minimum – maximum) values in the tables. Categorical variables were stated as number (n) and percentage (%). The variables were examined at a 95% confidence interval and a value of $p<0.05$ was accepted as statistically significant.

Results

The mean age of the patients was 33.66±5.56 years in Group P and 33.04±5.71 years in Group PK. The difference was not statistically significant (p=0.514). With respect to ASA status, no statistically significant difference was determined. ASA I was determined in 59 (58.4%) patients in Group P and 31 (56.4%) in Group PK. ASA II was determined in 42 (41.6%) in Group P and 24 (43.6%) in Group PK (p=0.866). With respect to the other demographic variables, no statistically significant difference was determined between the groups in mean bodyweight (Group P: 68.62±8.36 kg, Group PK: 67.93±11.12 kg) (p=0.671), mean height (Group P: 160 cm (172-155cm), Group PK: 160 cm (170-156cm)) (p=0437), or in the mean total duration of the procedure (Group P: 16 mins (24-12 mins), Group PK: 16 mins (28-11 mins)) (p=0.886).

The consumption of propofol throughout the operation was de-

termined as median 170 mg (range, 320-120 mg) in Group P and 140 mg (range, 190-110 mg) in Group PK and the difference was statistically significant (p<0.001). The recovery time of 6 mins (range, 3-9 mins) for Group P was statistically significantly shorter than that for Group PK of 7 mins (range, 5-10) (p<0.001).

In the evaluation of the embryological data, the values determined in Group P and Group PK respectively were estradiol (E2): 1343 (14759-168) and 1159 (6639-93), total oocyte count: 8 (57-1) and 7 (52-1), mature oocyte count(M2): 6 (43-0) and 5 (42-0), and fertilised oocyte count: 5 (35-1) and 4 (31-1). No statistically significant difference was determined between the groups in respect to these data (p=0.837, p=0.434, p=0.518, p=0.524 respectively). The pregnancy rates of patients were 32.7% (n=33) in Group P and 29.1% (n=16) in Group PK; the difference was not statistically significant (p=0.720). The demographic data of the patients in the study and all the other data are shown in Table 1.

Discussion

In this retrospective evaluation, the total propofol consumption for general anaesthesia was observed to be greater in the Group P patient group than in Group PK and the postoperative recovery period was shorter in Group P. The mean E2 levels, total, M2 and fertilised oocyte count values, and the pregnancy rates were found to be similar in both groups.

The OPU procedure applied for IVF is generally a short procedure and is applied with several anaesthesia methods. While regional methods with conscious sedation have advantages such as providing verbal communication with the patient and a lower incidence of respiratory tract complications such as aspiration and laryngo-bronchial spasm, the applications of deep sedation or general anaesthesia have been found to be superior in respect to preventing patient movements, facilitating ovarian aspiration with reduced uterus tonus, and removing anxiety [1, 5, 10]. In a study by Hong et al., the amount of propofol administered for conscious sedation in the OPU procedure in a high-anxiety group was found to be greater than that of a low-anxiety group [9].Therefore, as the majority of patients at our centre have high anxiety levels, deep sedation and general anaesthesia methods via a face mask were preferred for these patients.

However, in general anaesthesia, muscle relaxant and intubation with mechanical ventilator support cannot be applied. While the majority of IV anaesthetic agents can be used alone or together with inhalation agents, propofol, remifentanyl, and alfentanyl are used more often because of the short period of their effects and more rapid recovery [4]. In our clinic, propofol, ketamine, and remifentanyl are used together with sevoflurane as an inhalation agent. The aim here is to use the optimum dose of a combination of short-effect agents in OPU, a short duration intervention, and rapid recovery.

With the current applications of TIVA or target-controlled infusion (TCI) [10, 11], in our centre in particular, propofol is applied intermittently as IV push. Although TCI seems to be the most appropriate method, as the device is not available in our clinic, it is not applied. The TIVA method was not preferred as it was anticipated that difficulties could be experienced in making adjustments for the optimal dose due to the short duration of the procedure. Another reason was that with the use of a higher dose of propofol, there could be the possibility of follicular fluid transfer. In a study by Christiansen et al. 2mg/kg propofol was administered as IV push followed by 10mg/kg/hr infusion in the OPU procedure [12]. In another study investigating the effect of propofol in OPU on oocyte and early embryo quality, in a similar manner to the current study, a dose of 1.5-2mg/kg propofol was used in induction and, when necessary, repeated doses were applied by IV push [13].

Table 1. Comparison of demographic data and other data related to the procedure

	P		PK	Total	P Value
	(n=101)		(n=55)	(N=156)	
	Mean±SD.		Mean±SD.	Mean±SD.	
Age	33,66±5,56		33,04±5,71	33,44±5,60	0,514
Weight	68,62±8,36		67,93±11,12	68,38±9,39	0,671
	Median (Max.-Min.)		Median (Max.-Min.)	Median (Max.-Min.)	
Height	160 (172-155)		160 (170-156)	160 (172-155)	0,437
Total procedure time (min)	16 (24-12)	16 (28-11)	16 (28-11)	0,886	
Total propofol consumption (mg)	170 (320-120)	140 (190-110)	160 (320-110)	<0,001	
Recovery time (min)	6 (9-3)	7 (10-5)	6 (10-3)	<0,001	
E2 value	1343 (14759-168)		1159 (6639-93)	1321 (14759-93)	0,837
Total oocyte number	8 (57-1)	7 (52-1)	8 (57-1)	0,434	
Mature oocyte (M2) number	6 (43-0)	5 (42-0)	6 (43-0)	0,518	
Fertilized oocyte number	5 (35-1)	4 (31-1)	5 (35-1)	0,524	
ASA	n (%)		n (%)	n (%)	
I	59 (58,4)		31 (56,4)	90 (57,7)	0,866
II	42 (41,6)		24 (43,6)	66 (42,3)	
Pregnancy Rate					
No	68 (67,3)		39 (70,9)	107 (68,6)	0,720
Yes	33 (32,7)		16 (29,1)	49 (31,4)	

Independent T Test(Bootstrap) - Mann Whitney U Test(Monte Carlo) - Fisher Exact Test(Exact) - SD. :Standard deviation - Max. Maximum - Min. :Minimum
(p<0.05 value statistically significant)

Although recent studies have shown no harmful effects of propofol on oocytes [13, 14], earlier animal studies have shown negative effects [7, 15]. Similarly, there are studies that have shown negative effects of other IV anaesthetics and analgesics by the transfer of follicular fluid. Still other studies have shown no harmful effects [6, 16, 17].

It can be seen that there is not yet consensus on this subject. Although there have been fewer studies related to inhalation agents, it has been reported that halotane and isoflurane in particular have harmful effects on oocytes through the transfer of follicular fluid. However, it should be noted that they were animal studies and the surgical procedures applied were lengthy laparoscopic OPU methods [18-20]. Piroli et al. reported similar high rates of fertilisation using general anaesthesia with sevoflurane and with local anaesthesia methods in transvaginal OPU procedure [21]. In the current study, which was conducted retrospectively, the follicular fluid amounts were not measured because that is not a routine procedure for administering the anaesthetic agents.But, similar to other recent studies, fertilisation and pregnancy rates and the oocyte quality were not seen to have been significantly affected. It has been reported in previous studies that propofol and remifentanyl are suitable anaesthetic agents because of their positive effects in OPU anaesthesia [14, 22]. The same can be said for patients where ketamine was added. In a study by Ben-Sholomo et al. which compared the general anaesthesia method using propofol, fentanyl, and isoflurane with sedative anaesthesia using ketamine and midazolam, ketamine and midazolam were reported to be appropriate agents in OPU anaesthesia [23]. In the current study, the addition of ketamine slightly prolonged the postoperative recovery period, but this is offsetbythe reduction in propofol consumption. No abnormal event in the haemodynamic parameters was observed during or after the operation in any patient and no serious complication related to bleeding or the respiratory tract developed.

In conclusion, in OPU applied for IVF, the application of anaesthesia with propofol, ketamine, remifentanyl, and sevoflurane can be considered a suitable anaesthetic option for this patient groupas it did not have any negative effect on fertilisation.

Competing interests

The authors declare that they have no competing interests.

References

1. Sharma A, Borle A, Trikha A. Anesthesia for in vitro fertilization. J Obstet Anaesth Crit Care 2015;5(2):62-72.
2. Vhalos NF, Giannakikou I, Vlachos A, Vitoratos N. Analgesia and anesthesia for assisted reproductive technologies. Int J Gynaecol Obstet 2009;105(3):201-5.
3. Vasudevan B, Borle A, Singh PM, Ramachandran R, Rewari V, Trikha A. The effect of anesthetic technique for transvaginal ultrasound-guided oocyte retrieval on reproductive outcomes: A systematic review and meta-analysis. J Obstet Anaesth Crit Care 2015;5(2):54-61.
4. Matsota P, Sidiıopoulou T, Batistaki C, Giannaris D, Pandazi A, Krepi H et al. Analgesia with remifentanil versus anesthesia with propofol-alfentanil for transvaginal oocyte retrieval: A randomised trial on their impact on in vitro fertilization outcome. MEJ ANESTH 2012;21(5):685-92.
5. Yasmin E, Dresner M, Balen A. Sedation and anaesthesia for transvaginal oocyte collection: an evaluation of practice in the UK. Hum Reprod 2004;19(12):2942-5.
6. Soussis I, Boyd O, Paraschos T, Duffy S, Bower S, Troughton P et al. Follicular fluid levels of midazolam, fentanyl and alfentanil during transvaginal oocyte retrieval. Fertil Steril 1995;64(5):1003-7.
7. Janssenswillen C, Christiaens F, Camu F, Van Steirteghem A. The effect of propofol on parthenogenetic activation, in vitro fertilization and early development of Mouse oocytes. Fertil Steril 1997;67(4):769-74.
8. Circeo L, Grow D, Kashikar A, Gibson C. Prospective, observational study of the depth of anesthesia during oocyte retrieval using a total intravenous technique and the Bispectral index monitor. Fertil Steril 2011;96(3):635-7.
9. Hong JY, Jee YS, Luthardt FW. Comparison of conscious sedation for oocyte retrieval between low-anxiety and high-anxiety patients. J Clin Anesth 2005;17(7):549-53.
10. Edwards JA, Kinsella J, Shaw A, Evans S, Anderson KJ. Sedation for oocyte retrieval using target controlled infusion of propofol and incremental alfentanil delivered by non-anaesthetists. Anaesthesia 2010;65(5):453-61.
11. Murthy TVSP, Gupta P, Sharma RK. Anaesthetic issues in in-vitro fertilizations. MJAFI 2008;64(2):119-22.
12. Christiaens F, Janssenswillen C, Verborgh C, Moerman I, Devroery P, Steirteghem AV et al. Propofol concentrations in follicular fluid during general anaesthesia for transvaginal oocyte retrieval. Hum Reprod 1999;14(2):345-8.
13. Ben-Sholomo I, Moskovich R, Golan J, Eyali V, Tabak A, Shalev E. The effect of propofol anaesthesia on oocyte fertilization and early embryo quality. Hum Reprod 2000;15(10):2197-9.
14. Bümen S, Günüşen İ, Fırat V, Karaman S, Akdoğan A, Göker Tavmergen EN. A comparison of intravenous general anesthesia and paracervical block for in vitro fertilization: effects on oocytes using the transvaginal technique. Turk Med Sci 2011;41(5):801-8.
15. Alsalili M, Thornton S, Fleming S. The effect of anaesthetic, Propofol, on in-vitro oocyte maturation, fertilization and cleavage in mice. Hum Reprod 1997;12(6):1271-4.
16. Bruce DL, Hinkley R, Norman PF. Fentanyl does not inhibit fertilizations on early development of sea urchin eggs. Anesth Analg 1985;64(5):498-500.
17. Swanson RJ, Leavitt MG. Fertizilation and mouse embryo development in the presence of midazolam. Anesth Analg 1992;75(4):549-54.
18. Azmude A, Agha'amou S, Yousefshahi F, Berjis K, Mirmohammad'khani M, Sadaat'ahmadi F et al. Pregnancy outcome using general anesthesia versus spinal anesthesia for in vitro fertilization. Anesth Pain Med 2013;3(2):239-42.
19. Aghaamoo S, Azmoodeh A, Yousefshahi F, Berjis K, Ahmady F, Qods K et al. Does spinal analgesia have advantage over general anesthesia for achieving success in in vitro fertilization? Oman Med J 2014;29(2):97-101.
20. Chetkowski RJ, Nass TE. Isoflurane inhibits early Mouse embryo development in vitro. Fertil Steril 1988;49(1):171-3.
21. Piroli A, Marci R, Marinangeli F, Paladini A, Di Emidio G, Giovanni Artini P et al. Comparison of different anaesthetic methodologies for sedation during in vitro fertilization procedures: Effects on patient physiology and oocyte competence. Gynecol Endocrinol 2012;28(10):796-9.
22. Rosenblatt MA, Bradford CN, Boadian CA, Grunfeld L. The effect of a propofol-based sedation technique on cumulative embryo scores, clinical pregnancy rates, and implantation rates in patients undergoing embryo transfers with donor oocytes. J Clin Anesth 1997;9(8):614-7.
23. Ben-Sholomo I, Moskovich R, Katz Y, Shalev E. Midazolam/ketamine sedative combination compared with fentanyl/propofol/isoflurane anaesthesia for oocyte retrieval. Hum Reprod 1999;14(7):1757-9.

How to cite this article:
Urfalıoğlu A, Yaylalı A. Effect of Anesthetics During Oocyte Pick-Up Procedure on Oocyte Quality and Pregnancy. J Clin Anal Med 2016;7(6): 840-3.